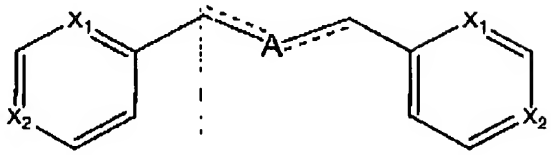
Appl. No.: 10/690,462
Amendment dated April 3, 2006
Reply to Office Action of November 3, 2005

Amendments to the Claims:

1-12. (Cancelled)

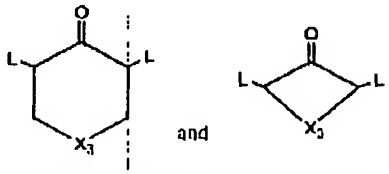
13. (Currently amended) A compound of the formula



wherein:

one of X_1 and X_2 is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



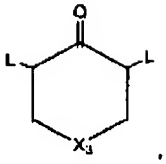
and

wherein X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of ~~H,~~ substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

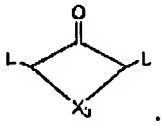
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof.

14. (Previously presented) The compound of Claim 13, wherein A is  .

15. (Previously presented) The compound of Claim 14, wherein X_3 is S or NR_1.

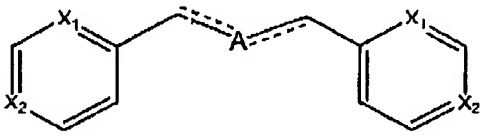
16. (Previously presented) The compound of Claim 13, wherein A is  .

17 - 19. (Canceled)

20. (Previously presented) The compound of Claim 13, wherein the optional double bonds are present.

21 - 22. (Canceled)

23. (Currently amended) A pharmaceutical formulation, comprising a compound of the formula

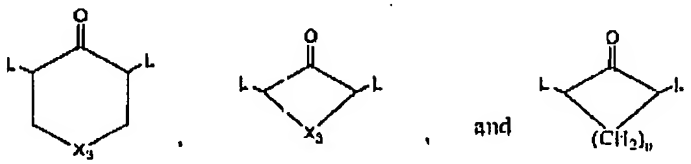


wherein:

one of X_1 and X_2 is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a

carboxylic ester group, a carboxamide group, nitro, cyano, azido, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



wherein n is 1-8; X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of ~~H,~~ substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

the dashed lines indicate the presence of optional double bonds;

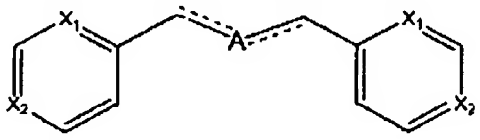
L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

24 - 25. (Canceled)

26. (Currently amended) A method of treating cancerous tissue in a subject, comprising administering to the subject an effective amount of a compound of formula

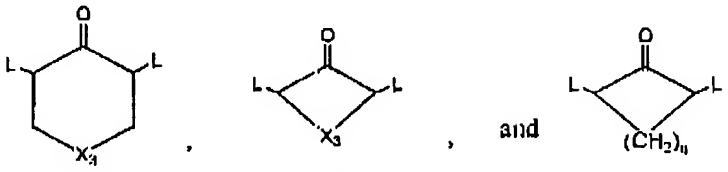


wherein:

one of X_1 and X_2 is nitrogen and the other is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a

carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



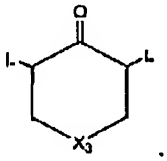
wherein n is 1-8; X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of ~~H, alkyl,~~ substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

the dashed lines indicate the presence of optional double bonds;

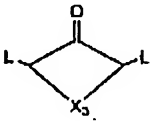
L is the point of bonding of A to the compound structure; or

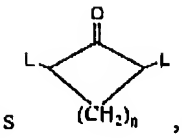
a pharmaceutically acceptable salt thereof;

wherein said cancerous tissue is selected from the group consisting of breast cancer, colon cancer, prostate cancer, skin cancer, leukemia, non-small cell lung cancer, CNS cancer, ovarian cancer, and renal cancer.

27. (Previously presented) The method of Claim 26, wherein A is  .

28. (Previously presented) The method of Claim 27, wherein X_3 is S or NR_1.

29. (Previously presented) The method of Claim 26, wherein A is  .

30. (Previously presented) The method of Claim 26, wherein A is  , wherein n is 1-4.

31 - 32. (Canceled)

33. (Previously presented) The method of Claim 26, wherein the optional double bonds are present.

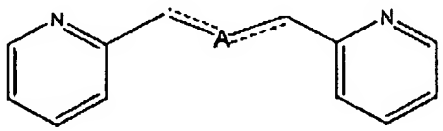
34 - 35. (Canceled)

36. (Currently amended) ~~A~~ The method of Claim 26, wherein the effective amount comprises an amount sufficient to inhibit VEGF production in the cancerous tissue.

37. (Currently amended) ~~A~~ The method of Claim 26, wherein the effective amount comprises an amount sufficient to inhibit TF production in the cancerous tissue.

38. (Currently amended) ~~A~~ The method of Claim 26, wherein said administering step comprises administering an effective amount of the compound in a pharmaceutically acceptable carrier.

39. (New) A compound of the formula

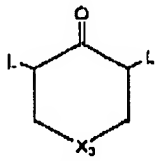
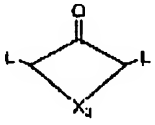


wherein:

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl,

alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:

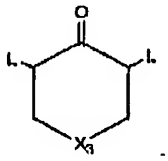

and


wherein X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

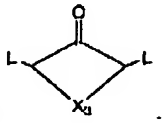
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof.

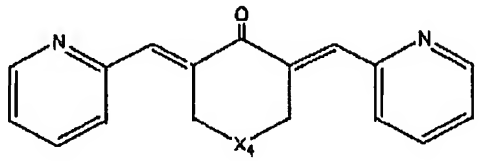
40. (New) The compound of Claim 39, wherein A is  .

41. (New) The compound of Claim 40, wherein X_3 is S or NR_1.

42. (New) The compound of Claim 39, wherein A is  .

43. (New) The compound of Claim 39, wherein the optional double bonds are present.

44. (New) The compound of Claim 39, having the formula



wherein:

X_4 is NR_1;

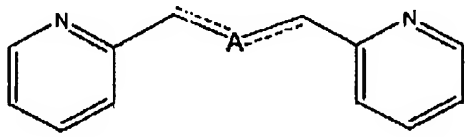
R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

or a pharmaceutically acceptable salt thereof.

45. (New) The compound of Claim 39, wherein the compound is 3-5-Bis-(2-pyridinylidene)-piperidin-4-one.

46. (New) A pharmaceutical formulation, comprising a compound of the formula

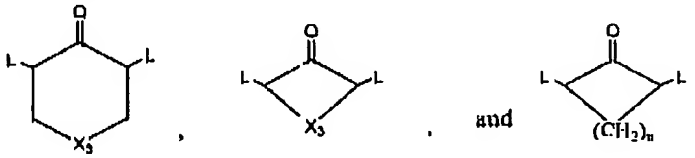


wherein:

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl,

heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



wherein n is 1-8; X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

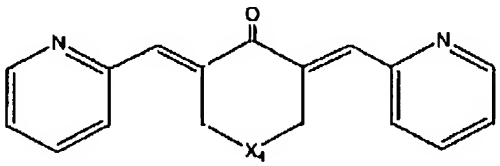
the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

47. (New) The pharmaceutical formulation according to claim 46, comprising a compound of the formula



wherein:

X_4 is NR_1;

R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

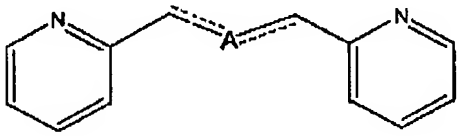
each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

48. (New) The pharmaceutical formulation according to claim 46, comprising 3-5-Bis-(2-pyridinylidene)-piperidin-4-one or 3,5-Bis-(2-pyridinylidene)-1-methylpiperidin-4-one, and a pharmaceutically acceptable carrier.

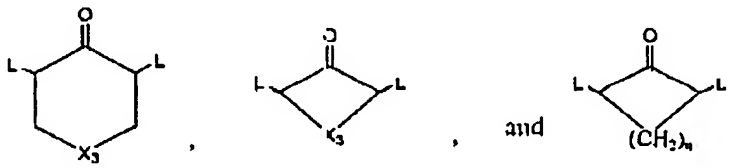
49. (New) A method of treating cancerous tissue in a subject, comprising administering to the subject an effective amount of a compound of formula



wherein:

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



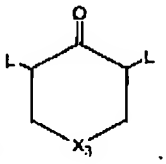
wherein n is 1-8; X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

the dashed lines indicate the presence of optional double bonds;

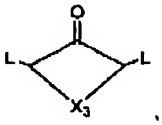
L is the point of bonding of A to the compound structure; or

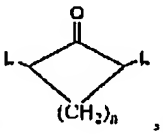
a pharmaceutically acceptable salt thereof;

wherein said cancerous tissue is selected from the group consisting of breast cancer, colon cancer, prostate cancer, skin cancer, leukemia, non-small cell lung cancer, CNS cancer, ovarian cancer, and renal cancer.

50. (New) The method of Claim 49, wherein A is  .

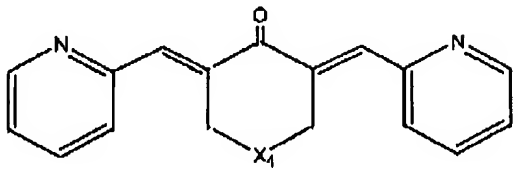
51. (New) The method of Claim 50, wherein X_3 is S or NR_1.

52. (New) The method of Claim 49, wherein A is  .

53. (New) The method of Claim 49, wherein A is  , wherein n is 1-4.

54. (New) The method of Claim 49, wherein the optional double bonds are present.

55. (New) The method of Claim 49, wherein the compound has the formula



wherein:

X_1 is NR_1;

R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl and dialkylaminocarbonyl;

each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

or a pharmaceutically acceptable salt thereof.

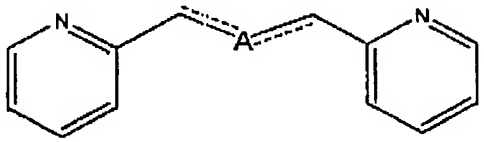
56. (New) The method of Claim 49, wherein the compound is selected from the group consisting of 3-5-Bis-(2-pyridinylidene)-piperidin-4-one and 3,5-Bis-(2-pyridinylidene)-1-methylpiperidin-4-one.

57. (New) The method of Claim 49, wherein the effective amount comprises an amount sufficient to inhibit VEGF production in the cancerous tissue.

58. (New) The method of Claim 49 wherein the effective amount comprises an amount sufficient to inhibit TF production in the cancerous tissue.

59. (New) The method of Claim 49, wherein said administering step comprises administering an effective amount of the compound in a pharmaceutically acceptable carrier.

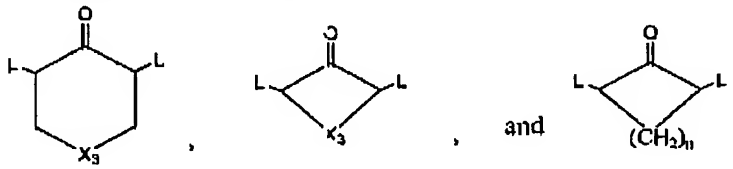
60. (New) A method of treating cancerous tissue in a subject, comprising administering to the subject an effective amount of a compound of formula



wherein:

X_1 is nitrogen and X_2 carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



wherein n is 1-8; X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

the dashed lines indicate the presence of optional double bonds;

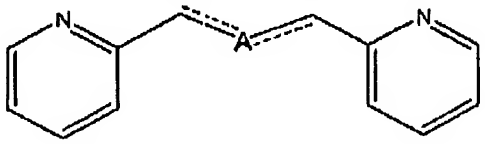
L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof;

wherein the effective amount comprises an amount sufficient to inhibit VEGF production in the cancerous tissue.

61. (New) The method of claim 60, wherein said cancerous tissue is selected from the group consisting of breast cancer, colon cancer, prostate cancer, skin cancer, leukemia, non-small cell lung cancer, CNS cancer, ovarian cancer, and renal cancer.

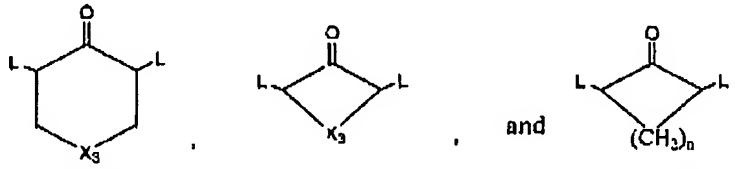
62. (New) A method of treating cancerous tissue in a subject, comprising administering to the subject an effective amount of a compound of formula



wherein:

X_1 is nitrogen and X_2 is carbon, wherein each carbon atom of the heteroaryl rings is optionally substituted with a substituent selected from the group consisting of halogen, hydroxyl, alkoxy, CF_3, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkaryl, arylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, amino, alkylamino, dialkylamino, a carboxylic acid group, a carboxylic ester group, a carboxamide group, nitro, cyano, azide, alkylcarbonyl, acyl, and trialkylammonium;

A is selected from the group consisting of:



wherein n is 1-8; X_3 is O, S, SO, SO_2, or NR_1; and R_1 is selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, acyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, and dialkylaminocarbonyl;

the dashed lines indicate the presence of optional double bonds;

L is the point of bonding of A to the compound structure; or

a pharmaceutically acceptable salt thereof;

wherein the effective amount comprises an amount sufficient to inhibit TF production in the cancerous tissue.

63. (New) The method of claim 62, wherein said cancerous tissue is selected from the group consisting of breast cancer, colon cancer, prostate cancer, skin cancer, leukemia, non-small cell lung cancer, CNS cancer, ovarian cancer, and renal cancer.